PMC49

THE ROLE OF PATIENT-REPORTED OUTCOMES (PRO) AS PRIMARY ENDPOINTS IN THE EVALUATION OF MEDICINES APPROVED WITH PRO CLAIMS

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OBJECTIVES: To review the drugs that used PRO as primary endpoints in the evaluation of their clinical efficacy and have been granted a PRO claim by the Food & Drug Administration (FDA) or the European Medicines Agency (EMA). **METHODS:** The PROLabels database, which centralizes medicinal products with a PRO claim, was searched using the keyword "primary endpoint". Only drugs approved between January 1, 1995 and May 28, 2010 were included. **RESULTS:** A total of 303 (66%) out of the 459 products included in the database were retrieved: four were removed because of a withdrawal notice (all EMA), 15 because they were approved before 1995, and two others because the endpoints were not clearly specified. In total, 282 products were analyzed (71 approved in Europe). They represented 81 different indications, with 47 products having more than one indication. The most frequent indications were: Pain (25 products), Rheumatoid Arthritis (25), Menopause (18), Parkinson's disease (17), Epilepsy (15), Migraine disorders (13), Sleep disorders (12), Rhinitis Allergic Perennial, Seasonal (12), and Ankylosing Spondylitis (10). In total, 140 different PRO endpoints were listed. Seventy-seven percent of them were symptoms (e.g. pain, bowel movement, heartburn symptoms, asthma symptoms, etc). Function (e.g. physical function, functional impairment, etc) represented only 5.7% of all endpoints. Health-related quality of life (HRQL) was a clear primary endpoint in only two products: Duloxetine (Urinary Incontinence) and Alisade (Rhinitis Allergic Perennial and Seasonal). Both approvals were granted by the EMA in 2008 (after the first publication of the EMA and FDA guidances). **CONCLUSIONS:** Symptoms, as measured by patients, are a key criterion in the evaluation of medicines. Unsurprisingly, pain is the main indication in which the highest number of products with a PRO as a primary endpoint are approved. More sophisticated PRO endpoints, such as function or HRQL, are used less often.

PMC50

TRANSLATION, LINGUISTIC VALIDATION AND ELECTRONIC ADMINISTRATION IN THE INDIAN LANGUAGES: A CASE STUDY HIGHLIGHTING THE SPECIAL DIFFICULTIES THAT EXIST AT THIS INTERSECTION

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OBJECTIVES: Translation and linguistic validation of questionnaires for paper or electronic administration require similar procedures. Both modalities share a common difficulty: how to best utilize existing processes to accommodate Indian languages. Working with Indian language instruments can be daunting, even without the compounded effect of managing both ePRO and linguistic validation together. This paper seeks to enumerate the challenges associated with the intersection of Indian languages, linguistic validation, and electronic administration and recommends the use of a specialized checklist to avoid escalating potential difficulties. **METHODS:** A case study was performed to explore the complexity of these processes. a Fibromyalgia e-diary and corresponding paper diary were translated into four Indian languages and three non-Indian languages with varying levels of linguistic difficulty. This allowed for a multidimensional analysis of issues faced in translation for ePRO versus paper administration, and translation for Indian versus non-Indian settings. **RESULTS:** During linguistic validation, difficulties arise pertaining to font and formatting requirements, localization of colloquial terms and phrases and maintaining concept equivalency while respecting cultural appropriateness. Preparing an ePRO for use involves thorough analysis of existing instrument versions and possible modification of instructions, response sets or questionnaire format to accommodate technology or screen size limitations. a holistic approach of quality assurance should be employed, including multiple rounds of proofreading. When preparing an Indian language for electronic administration one must take even more care, accounting for the factors listed above as well as considering software font-testing prior to production, and additional proofreading steps. **CONCLUSIONS:** Linguistic validation of ePRO questionnaires for use in Indian settings presents special challenges. Evidence suggests that additional consideration must be exercised early on in order to avoid compounded difficulties and delays later in the process. In such cases, the use of a checklist is recommended to assist in preempting future difficulties within the project.

PMC51

CONCEPT ELABORATION—AN ESSENTIAL STAGE IN THE TRANSLATION OF PRO MEASURES

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The ISPOR Principles of Good Practice paper for the translation of patient-reported outcome (PRO) measures describes concept elaboration within the scope of project preparation and emphasises that the misinterpretation of items or concepts can result if the step is not undertaken. However, the paper does not discuss how to correctly perform concept elaboration or why it is an essential step in the translation process. Translation companies often harmonise their own translations with each other, but not with existing translations. Over time, a single measure may be translated by any number of companies. Wording choices are often made by various translators and project managers without prior guidance—this can lead to wide variations. a concept elaboration document approved by the developer provides consistent clarification and guidance to promote harmonization across all language versions regardless of who is carrying out the work. Inconsistent wording choices across language versions can be due to misunderstandings as a result of ambiguous wording in the source text, misinterpretation of idioms or the influence of personal choice resulting in inconsistent use of alternative phrases for terms that are not directly translatable. Concept elaboration remedies these issues by providing a line-by-line analysis of the source text which clarifies ambiguous wording, provides alternative wording for items with no direct translation, recommends suitable equivalents of culture-bound concepts and provides guidelines on nuance, tone, and emphasis. Concept elaboration ensures that the text is fully understood by all translators before any translation work begins. It encourages standardised decision making for every language and allows the developer to exercise influence over the style and content of the translations even if they are unable to review each translation individually. For studies including developer reviews, these reviews should become more straightforward as the translations will have been carried out according to the developer's guidance.

PMC52

TREATMENT SATISFACTION WITH MEDICATION: A REVIEW OF CONCEPTUAL FRAMEWORKS AND APPLICATIONS

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OBJECTIVES: The construct of treatment satisfaction with medication (TS-M) provides an avenue for incorporating the patients' voice in treatment evaluation. In recent years, due to the growing influence of the consumer in health care decisions, there have been a substantial number of both generic and disease-specific TS-M instruments developed. This study provides a review of the available TS-M measures and examples of its applications. **METHODS:** A literature review was conducted using MEDLINE, ISPOR Research Digest and Google Scholar to identify generic and disease-specific TS-M instruments as well as any applications of these instruments. The review included evaluation of research articles, abstracts, review articles, news articles and editorials discussing instruments that measure TS-M. **RESULTS:** A total of 39 instruments that measure TS-M were identified. Out of the 39 instruments, four instruments were generic in nature that could be used across therapy areas and included the three versions of the Treatment Satisfaction Questionnaire for Medication (TSQM) (TSQM v1.4, TSQM vII, TSQM-9) and the SATMED-Q. The rest of the 35 measures were disease-specific TS-M instruments covering many diseases including migraine, pain, HIV, diabetes, Crohn's disease, oncology, osteoarthritis, men's health and multiple sclerosis. The instruments varied substantially in the number of items and domains they covered and included anywhere from 6 items to 46 items. Treatment satisfaction data has been used to inform clinician decision-making, support label claims, and for supporting the marketing of drugs. For example, in the past decade, TS-M has been used to support label claims for 17 products in Europe and in marketing effort of drugs in many therapy areas including erectile dysfunction, heart disease and diabetes. **CONCLUSIONS:** Treatment satisfaction with medication can be an important endpoint for product differentiation of novel treatments. Among the existing TS-M instruments, researchers could benefit by identifying instruments that have been developed using psychometrically rigorous standards and procedures.

PMC53

COMPARISON OF METHODS FOR ITEM GENERATION AND PRETESTING OF FIVE LYMPHOEDEMA-SPECIFIC HEALTH-RELATED QUALITY OF LIFE QUESTIONNAIRES

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OBJECTIVES: A systematic literature review identified four patient-reported outcome (PRO) measures that have been used in the assessment of quality of life for patients with upper limb lymphoedema. These are in addition to the author's newly devised questionnaire. However the developers had all used different methods to devise the items with the final measures incorporating different items and domains. The objective was to compare the methods that had been used and review in the light of available guidance on best practice. **METHODS:** Review and tabulate the available information on each PRO regarding its development. Key aspects of the evaluation included specificity of target population, source of item generation, number of initial items generated, drafting of item/question wording, pretesting and defining the domains. **RESULTS:** Two of the five PROs had been developed to assess the quality of life of patients with upper or lower limb lymphoedema decreasing the specificity of the target population; two of the PROs did not use patients as the source for items relying on clinicians; the number of items initially generated by the remaining three PROs were 98, 134 and 495, but none of the developers evaluated the point of saturation; different approaches were used for analyses of the items generated to create the initial draft of items/questions; not all PROs were pretested. Number of domains ranged from two to seven and number of items/questions in initial drafts ranged from 5 to 70. **CONCLUSIONS:** Each of the PROs measuring the same concept have been developed using different methods of generating the items and pretesting an initial draft of the PRO. To advance the field of measuring quality of life of lymphoedema patients, it will be important to establish which PRO measure has the best validity, that is, best reflects the impact of lymphoedema on their health and well-being.